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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,271	01/22/2001	Gil H. Choi	PB340P2C3	9691

22195 7590 05/06/2003

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EXAMINER
DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/765,271	Choi et al
Examiner	**Group Art Unit**
DUFFY	1645

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 1-28-03.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1-29 is/are pending in the application.

Of the above claim(s) 10, 11, 12, 14-21 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-9 + 13 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-21 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☒ Other Sequence notice to comply

Office Action Summary

DETAILED ACTION

1. The response filed January 28, 2003 has been entered into the record.

Sequence Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. For example, on pages 10 and 11 a peptide sequence is recited but is not followed by a proper sequence identifier and is not separately listed in a sequence listing. Full compliance with the sequence rules is required in response to this office action. Failure to fully comply with the sequence requirements in the time period set forth in this office action will be held non-responsive.

Priority

3. If applicant desires priority under 35 U.S.C. 119(e) or 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should

follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Specification

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Information Disclosure Statement

5. No information disclosure statement has been filed in this application.

Election/Restriction

6. Applicant's election with traverse of Group 1, SEQ ID NOS:55 and 56 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the members of the Markush group are sufficiently few in number or so closely related that a search and examination of all the claims of the entire application can be made without serious burden and that even though patentably distinct inventions appear in a single application, restriction remains improper unless the examiner can show that the search and examination of these groups would entail a "serious burden". Applicant's arguments have been fully considered but are not found to be fully persuasive.

This is not found persuasive because the term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of Groups I=VI

and all Markush members are drawn to distinct inventions which are related as separate products capable of separate manufacture, use or sale as described in the previous Office Action. Restrictions between the inventions is deemed to be proper for the reasons previously set forth. In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. In the instant case a burden has been established in showing that the inventions of Groups I-VI are classified separately necessitating different searches of issued U.S. Patents. However, classification of subject matter is merely one indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive. A reference which would anticipate the invention of one group would not necessarily anticipate or make obvious any of the other groups. Furthermore, MPEP 803.04 sets forth that biological molecules with different sequences are separate inventions. A single sequence encoding a single polypeptide is a reasonable number based, upon the fact that each separate nucleic acid sequence encodes a distinct biological protein with a separate primary, secondary, and tertiary structure, as well as distinct biological activity and function. Clearly different searches and issues are involved in the examination of each Group. As such, search and examination of all the disparate unrelated proteins and nucleic acids of the claims would present a "serious burden".

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-9 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

It is noted that SEQ ID NO:55 is a genomic DNA fragment. The specification does not disclose that SEQ ID NO:55 is drawn to a full length open reading frame. The claims reciting "comprising" and "encoding" language read upon complete gene sequences having in

common a nucleotide sequence of SEQ ID NO:55 from any source. The claims also encompass polypeptide and polynucleotide variants, hybridizing variants and nucleic acid encoding epitopes. With the exception of SEQ ID NO:55, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the simplicity of the method of isolation, absent further guidance. Since the claimed genus encompasses undisclosed genes, partial genomic sequences, and genes yet to discovered, and variants thereof, the disclosed structural feature (i.e., the nucleic acid consisting of SEQ ID NO:55 encoding a polypeptide consisting of SEQ ID NO:56) does not constitute a substantial portion of the claimed genus. Absent a written description disclosing a representative number of nucleic acid sequences from this broad class of polynucleotides, the specification fails to show that applicant was "in possession of the claimed invention" at the time the application for patent was filed. In addition, claim 2 recite a nucleic acid comprising a nucleotide sequence comprising a sequence which specifically hybridizes to a nucleic acid comprising a sequence as set forth in SEQ ID NO:55 or variant thereof as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature of the instantly recited nucleic acids, nor a correlation between a particular structure and function. The genus of nucleic acid probes which would hybridize to a nucleic acid comprising SEQ ID NO:55 is very large, encompassing not only sequences with polymorphisms and mutations compared to SEQ ID NO:55, but also sequences having no shared sequence with SEQ ID NO:55 itself since the hybridization could occur within the non-SEQ ID NO:55 portion of the nucleic acid comprising SEQ ID NO:55 or encoding SEQ ID NO:56. Further, no function is required of this hybridizing nucleic acid. Thus the genus of nucleic acids encompassed by this claim is extensive, and there does not appear to be any requirement

that the nucleic acid probes share either a particular structure, a particular function, nor a correlation between some partial structure and a particular function. Consequently, SEQ ID NO:55 again does not appear to constitute a substantial portion of the claimed genus. Since these various nucleic acids do not possess defined structures, fragments of these nucleic acids also lack adequate written description, as do vectors, host cells, and associated methods using such. The genus of nucleic acids encompassed by the instant claims is much more extensive than SEQ ID NO:55 itself or internal fragments of SEQ ID NO:55 that could be used as probes or primers. The instant claim language opens up the claims to "flanking" sequences of undisclosed structure/sequence and unlimited length and variants within that structure that encode polypeptides or polynucleotides not disclosed in the specification. It is because of this open language that the specification fails to provide an adequate written description of the instant claims. However, the mere statement that a genus of nucleic acids is part of the invention and reference to a potential method for isolating some of these nucleic acids is not adequate written description of those nucleic acids. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Consequently, Applicant was not in possession of

the instant claimed invention. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (See page 1115.) Further, Reagents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398, appears to be directly relevant to the instant fact pattern. In Eli Lilly the specification and generic claims to all cDNAs encoding for vertebrate or mammalian insulin did not describe the claimed genus because they did not set forth any common features possessed by members of the genus that distinguished them from others. Id. at 1568, 43 USPQ2d at 1405. Nor did the specification describe a sufficient number of species within the very broad genus to indicate that the inventors had made a generic invention, i.e., that they had possession of the breadth of the genus, as opposed to merely one or two such species. Id. In the instant case, Applicant has described a single species (the nucleic acid consisting of SEQ ID NO:55), but is attempting to claim an extremely broad genus of nucleic acids which do not necessarily share any common feature with SEQ ID NO:55.

10. Claims 1-9 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide consisting of SEQ ID NO: 55, specific fragments thereof, vectors and host cells consisting of these, it does not reasonably provide enablement for an isolated polynucleotide comprising SEQ ID NO: 55 or a nucleic acid sequence encoding an amino acid sequence comprising SEQ ID NO:56 or epitope bearing portions thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's specification (page 5, lines 17-37) sets forth that the polynucleotide of the invention can be used diagnostically. However, such a detection is limited to consisting of SEQ ID NO: 55 or specific fragments thereof, since the addition of an indefinite

number of nucleotides 3' and 5' to SEQ ID NO:55 would unpredictably effect the ability to use SEQ ID NO:55 in a well established manner. Applicant's have not demonstrated that large sequences comprising SEQ ID NO:55 have this ability. Moreover, it is clear from a comparison of SEQ ID NO:55 with the art, that SEQ ID NO:55 encodes only a fragment of a larger protein. In the absence of the disclosure of a complete open reading frame, one skilled in the art would have reason to doubt that the protein of SEQ ID NO:56 is even produced by the bacterium. In the absence of the complete open reading frame, one of skill would have reason to doubt the production of the polypeptide by the bacterium and its asserted use as a diagnostic or use to make antibodies for diagnostic purposes. The specification fails to teach the activity or function of SEQ ID NO:56. The essential element of the claims are a bacterial polypeptide or bacterial antigen or epitope that is the full length open reading frame which is essential to the operation/function of the invention or the well established use as a bacterial antigen. The instant specification does not provide functional or structural characterization of the full length open reading frame of the instantly claimed bacterial polypeptide and polynucleotide which encodes the polypeptide. The specification does not provide a clear protocol by which the bacterial antigen comprising SEQ ID NO:56 was isolated from the microorganism of interest at the time the invention was made. The specification does not provide structural characterization of the complete open reading frame of the bacterial antigen (both start and stop codons). In the instant case, the classical start codon, methionine, is missing from the beginning of the bacterial polypeptide of SEQ ID NO:56. Absent characterization of the start codon, the genus of bacterial polynucleotides encoding proteins comprising SEQ ID NO:56 or fragments thereof is highly variant. One cannot enable that which one has not described. It is known for nucleic acids as well as proteins, for example, that even a

single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances (e.g, hemoglobin of sickle cell anemia involves a single amino acid substitution of valine for glutamate), albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Further, the specification fails to teach any function for the polypeptide such that one skilled in the art would be able to screen for functionally equivalent variants and no guidance is provided by the specification as to those substitutions that could be made. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the DNA of SEQ ID NO:55, which encodes the protein fragment of SEQ ID NO:56, is insufficient to describe the genus of nucleic acids comprising SEQ ID NO:55, variants, epitopes and hybridizing nucleic acids. Thus, Applicant's have not described a function which would adequately describe the genus of nucleic acids or the genus of polypeptide. One of skill in the art would reasonably conclude that the disclosure as filed fails to provide a representative number of species to describe the genus. Thus, applicant is not enabled for the claimed genus and it would require undue experimentation to make an use such.

Therefore, only an isolated polynucleotide consisting of SEQ ID NO:55, consisting of particular fragments of SEQ ID NO:55, vectors and host cells, but not the full breadth of the claim is enabled by the instant specification.

11. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's claim language encompasses methods of producing proteins encoded by a strand complementary to the coding sequence. One of skill in the art would be unable to practice such a claim. Complementary is routinely used in the art to describe the opposite (reverse complement) strand of a given DNA sequence (e.g., page 608, lines 5-6 of paragraph 1, Watson et al "Molecular Biology of the Gene" 4th Edition (1987) Benjamin-Cummings Publishing Company, Inc. USA), therefore the claims read upon a method of producing a polypeptide encoded by a sequence antisense to the coding strand. It is well known that antisense sequences do not encode products related to the sense strand, for example, the 5'-3' directionality is reversed, and therefore each codon triplet is read in the reverse orientation (encoding a different amino acid in most instances) and the N and C terminal of the encoded product is reversed. Applicant has not provided any guidance or working examples which would lead one of skill in the art to predict, first, that the antisense of SEQ ID NO:55 does, in fact, encode a protein product (e.g., start sequences, methionine codon, a substantial open reading frame, stop and other termination signals). Further one of skill in the art would not predict such a product would be structurally or functionally related, and Applicant has not provided any potential means of using such an unrelated protein.

In view of the lack of guidance, lack of working examples, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

12. Claims 1-9 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the instant case the claims are rendered indefinite from the inclusion of non-elected subject matter. Correction is required.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Birkett et al (U.S. Patent Number 5,302,527) or Boehringer Mannheim 1991 Catalog or Stratagene 1991 Product Catalog.

The claim is drawn to an isolated polynucleotide comprising a nucleic acid sequence which hybridizes under stringent conditions to SEQ ID NO:55, encoding variant or 95% identical variant or the complementary strand.

Birkett et al (U.S. Patent Number 5,302,527) disclose of random priming with a mixed hexamer oligonucleotide kit (Multiprime Kit, Amersham). (See column 15 lines 25-30). In view that the random hexamer oligonucleotides comprise every possible combination of six consecutive nucleotides and that these sequences will inherently

hybridize to the recited sequences under the recited conditions, the disclosure of the hexamer kit by Birkett et al is seen to anticipate the claimed invention.

Boehringer Mannheim Biochemicals teach isolated random primers (6-mers) for random priming of DNA. These sequences will inherently hybridize to the recited sequences under the recited conditions.

Stratagene 1991 product catalog teachs random 9-mer primers for random priming of DNA. These sequences will inherently hybridize to the recited sequences under the recited conditions.

Status of Claims

14. No claims are allowed.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.

May 2, 2003

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600